not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 7, 9-10 and 15-19 will pending.

Drawings:

The Examiner stated that the drawings filed in this application are objected to by the Draftsperson under 37 C.F.R. §§ 1.84 or 1.152 as indicated. The Examiner stated that these drawings are acceptable for examination purposes only. The Examiner stated that formal drawings with the appropriate corrections will be required when the application is allowed. The Examiner stated that applicant's are reminded to amend the specification (i.e., brief description of the figures including panel descriptions) if necessary when submitting corrected drawings.

In response, applicants will submit new drawings upon the indication of allowable subject matter.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 9 and 10 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that the reference to a "CD+ cell" is vague and indefinite since this does not appear to reference an art-recognized cell type and there is no definition of such a cell type in the specification. The Examiner stated that accordingly, the metes and bounds of the patent protection desired cannot be ascertained. The Examiner stated that applicants may obviate the rejection by directing the claim language toward "CD4+ cell".

In response, applicants have herein amended claims 9-10 such that they now recite **CD4+** cell [emphasis added]. Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 7-14 under 35 U.S.C. § 112, first paragraph alleging that the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The Examiner stated that the legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex pate Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The Examiner stated that the courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. The Examiner stated that *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The Examiner stated that the disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows: 1) The breadth of the claimed invention is exceedingly large and fails to receive adequate support in the specification. The Examiner stated that the claims do not provide any structural

limitations whatsoever on the inhibitory agent. The Examiner stated that thus, any chemical compound, including *inter alia*, organic compounds, peptide mimetics, and antibodies, may be encompassed by the claims. The Examiner stated that however, the specification fails to guide the skilled artisan toward these compounds that can reasonably be expected to retain the desired inhibitory activity. 2) The Examiner stated that the disclosure fails to provide sufficient guidance pertaining to the structural characteristics of those compounds that are capable of inhibiting macrophage-or T-cell-tropic isolates in a specific manner. The Examiner stated that the disclosure in silent pertaining to the identification of a common inhibitor motif in the agent of interest. 3) The Examiner stated that the disclosure also fails to provide any guidance pertaining to the molecular determinants of those regions of the viral envelope and cell surface receptor that are involved in fusion. The Examiner stated that this might enable the skilled artisan to rationally direct molecules toward certain active sites in the fusion reaction. The Examiner stated that however, without sufficient guidance pertaining to a suitable molecular target, the skilled artisan has only been extended an undue invitation to further experimentation to try to ascertain which compounds might function in the desired manner. The Examiner stated that the prior art is unpredictable and fails to provide sufficient illumination pertaining to the structural constraints governing viral-cell fusion. The Examiner stated that the most successful antiviral agents have been direct against well-characterized enzymatic sites (Hirsch et al. 1997). The Examiner stated that for instance, protease inhibitors are directed toward an enzymatically active site that has been identified through x-ray crystallography structures of the enzyme. The Examiner stated that

however, no such guidance is available for the current target of interest. 5) The Examiner stated that the disclosure fails to provide sufficient working embodiments to enable the breadth of the claimed invention. 6) The Examiner stated that legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 1824(C.C.P.A.) 1970). *In re Vaeck*, 20 U.S.P.Q. 2d 1438 (C.A.F.C.) 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). The Examiner stated that thus, when all the aforementioned factors are considered in *toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants contend that claimed invention is fully enabled and that undue experimentation was not required. Applicants contend that one skilled in the art can follow the methodology presented in the subject application to identify agents capable of specifically inhibiting fusion of a macrophage-tropic primary isolate of HIV-1 to a CD4+ cell.

In support, applicants attach hereto as **Exhibit B** a paper by William Olson et al. entitled "Differential Inhibition of Human Immunodeficiency Virus Type 1 Fusion, gp120 Binding, and CC-Chemokine Activity by Monoclonal Antibodies to CCR5" which describes in the bridging paragraph on pages 4146-4147 the identification of agents which inhibit HIV-1_{JR-FL} envelope mediated fusion with a PM-1 cell (e.g. a CD4+ cell) using the RET assay (i.e. the assay described in the subject applicant). The RET assay

is described on page 4146 in the section entitled "Inhibition of envelope-mediated membrane fusion and HIV-1 entry by anti-CCR5 Mabs." In further support, applicants attach hereto as **Exhibit C** a copy of published PCT International Application No. PCT/US99/30345, filed December 16, 1999 which describes on page 26 that such agents were identified using the RET assay. Accordingly, applicant's specification describes an assay (i.e. the RET assay) which enables one skilled in the art to identify agents which inhibit fusion of a macrophage-tropic primary isolate of HIV-1 to a $CD4^+$ cell. Accordingly, one skilled in the art can practice the claimed invention by following the teachings in the application and therefore, the claimed invention is enabled.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 11-14 under 35 U.S.C. § 102(b) as being anticipated by *Vanini et al.* (1992). The Examiner stated that this teaching discloses the preparation and characterization of syncytia-inhibiting affinity-purified antibodies and their methods of use. The Examiner stated that these antibodies are capable of inhibiting fusion between a T-cell tropic HIV-1 isolate (designated LAV) and CD4+ cells. The Examiner stated that thus, absent evidence to the contrary, this agent appears to meet all of the claimed limitations.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants respectfully point out that the agents of the claimed invention specifically inhibit fusion of a **macrophage-tropic** primary isolate of HIV-1 to a $CD4^+$ cell, **but not** a **T cell-tropic** isolate of HIV-1 to a $CD4^+$ cell. The antibodies described in Vanini are anti-gp41 antibodies which block fusion of

both macrophage tropic and T cell tropic isolates. In support, applicants attach hereto as **Exhibit D** a copy of a paper by Trkola et al. entitled "Neutralization Sensitivity of Human Immunodeficiency Virus Type 1 Primary Isolates to Antibodies and CD4-Based Reagents is Independent of Coreceptor Usage." This paper describes the neutralization of various HIV-1 strains by monoclonal antibodies and CD4-molecules. One of the antibodies tested is 2F5, which binds to the HIV envelope glycoprotein gp41 (see Purtscher et al. "Restricted antigenic variability if the epitope recognized by the neutralizing gp41 antibody 2F5" attached as **Exhibit E**). Applicants point out that gp41 is the same target as the antibody described in the cited reference (i.e. Vanini et al.). Trkola demonstrates in Table 1 and Figure 1 that the 2F5 antibody neutralizes **both** NSI strains (i.e. macrophage tropic strains) and SI strains (i.e. t-cell tropic strains) [emphasis added]. In contrast, the claimed invention recites an "agent determined to be capable of specifically inhibiting fusion of a macrophage-tropic primary isolate of HIV-1 to a $CD4^+$ cell, **but not** a T cell-tropic isolate of HIV-1 to a $CD4^+$ cell..." [emphasis added]. Since the Vanini antibodies block T-cell tropic HIV-1 isolates, they do not anticipate the claimed invention. Therefore, Vannini et al. does not anticipate the invention of claims 11-14. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 11-14 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application. Applicants contend that these remarks and amendments obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. § 102 (a)

The Examiner rejected claims 7-10 under 35 U.S.C. § 102(a) as being anticipated by Verrier et al. (1997). The Examiner stated that applicants are advised that priority cannot be extended to application Serial No. 08/475,515, filed June 7, 1995 and accordingly, the effective filing date for the purposes of applying art is that of Application Serial no. 08/973,601, filed March 16, 1998. The Examiner stated that Verrier discloses the preparation and characterization of syncytia-inhibiting affinity-purified antibodies and their methods of use. The Examiner stated that these antibodies are capable of inhibiting fusion between a macrophage-tropic HIV-isolate (designated Bx08) and CD4+ cells. The Examiner stated that these reagents do not affect fusion between T-cell-tropic isolates. The Examiner stated that thus, absent evidence to the contrary, this agent appears to meet all of the claimed limitations.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants maintain that they are entitled to the benefit of the filing date of U.S. Serial No. 08/475,515, i.e. June 7, 1995. Moreover, applicants are certainly entitled to the benefit of the filing date of PCT International Application No. PCT/US96/09894 (i.e. June 7, 1996) since the subject application is a national stage application filed under 35 U.S.C. §371 of such PCT application. Applicants respectfully point out to the Examiner that the first issued filing receipt contained incorrect information and request that he review the most recently issued filing receipt which contains the proper priority information. Since Vennier et al. was published in August 1997 (i.e. after June 7, 1996), it is

not a proper reference under 35 U.S.C. §102(a). Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

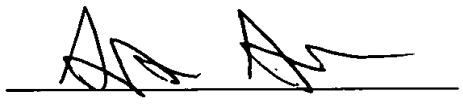
Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. 7, 9-10, and 15-19.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee, other than the enclosed $485.00 fee including the $445.00 fee for a three-month extension of time and the $40.00 fee for additional claims, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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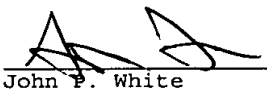
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



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